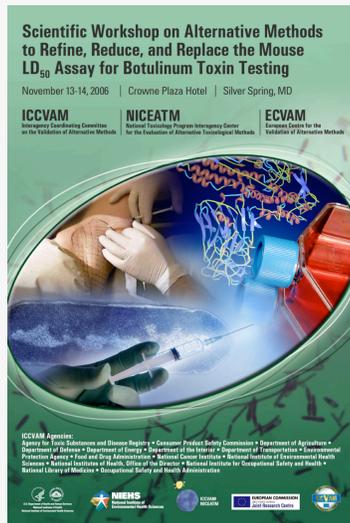


NICEATM

*National Toxicology Program
Interagency Center for the Evaluation of
Alternative Toxicological Methods*

ICCVAM

*Interagency Coordinating Committee on
the Validation of Alternative Methods*



ICCVAM/NICEATM/ECVAM Scientific Workshop on Alternative Methods to Refine, Reduce, and Replace the Mouse LD₅₀ Assay for Botulinum Toxin Testing

Introduction and Welcome

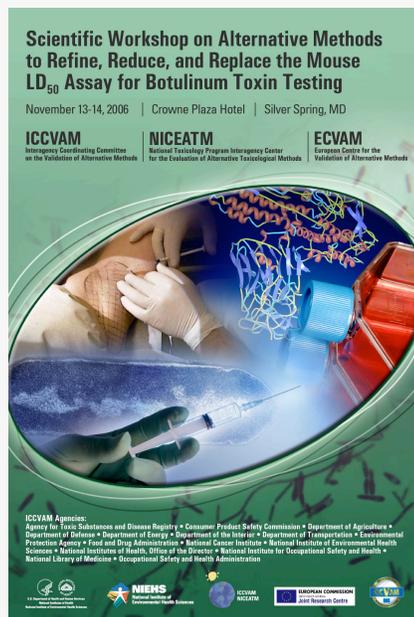
**William S. Stokes, D.V.M., DACLAM
RADM, U.S. Public Health Service**

November 13-14, 2006

**Crowne Plaza Hotel
Silver Spring, MD**



Workshop Organizers and Sponsors



- Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)
- National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM)
- European Centre for the Validation of Alternative Methods (ECVAM)



Background - 1

- **Oct 05: Nomination from HSUS to ICCVAM**
 - Convene an expert workshop to review existing alternative methods for botulinum toxin testing
 - ICCVAM should work with appropriate partners to validate one or more alternative assays
- **Nov-Dec 05: ICCVAM and SACATM endorsed as a high priority**
 - ICCVAM Biologics Working Group (BWG) established to organize the workshop

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Background - 2

- **Jan 06: *Federal Register* notice**
 - Requested:
 - Comments on the HSUS nomination
 - Nomination of experts
 - Submission of *in vivo* and *in vitro* data
 - 2946 responses received
 - All supported the proposed workshop
 - Nominations of experts and publications
- **Aug 06: *Federal Register* notice**
 - Announced workshop dates and agenda

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Workshop Goals

- To review the state-of-the-science and current knowledge of alternatives that may reduce, replace, and refine (less pain and distress) the use of mice for botulinum toxin testing
- To identify priorities for research, development, and validation efforts needed to advance the use of alternative methods

Workshop Objectives - 1

1. Review the public health needs for botulinum toxin testing, including the necessity to determine the safety and efficacy of products containing botulinum toxin (**Session 1**)
2. Review the current state-of-the-science and identify knowledge gaps regarding botulinum toxin structural aspects, mechanisms, and modes of action that are important to the development of alternative methods for *in vivo* botulinum toxin tests, and prioritize future research initiatives that would address these knowledge gaps (**Session 2**)

Workshop Objectives - 2

3. Review current development and/or validation status of alternative test methods for *in vivo* botulinum toxin tests and their potential to reduce, refine (less pain and distress), or replace the use of the mouse LD₅₀ assay (**Sessions 3, 4, and 5**)
4. Identify alternative methods that should have the highest priority for future development and validation studies to assess potency/toxicity of botulinum toxin (**Sessions 3, 4, and 5**)

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Workshop Agenda - Day 1

- **8:30-8:40 Introduction**
- **8:40-10:10 Session 1**
 - Overview of Public Health Needs for Botulinum Toxin Testing and Regulatory Requirements
- **10:30-11:30 Session 2**
 - Current Understanding and Knowledge Gaps for Botulinum Testing
- **11:30-12:30 Lunch**
- **12:30-2:05 Session 2 (cont'd)**
- **2:05-5:00 Session 3**
 - Potential Replacement of Animal Use for Botulinum Toxin Potency Testing
- **5:00-6:00 Poster Session**

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Workshop Agenda - Day 2

- **8:30-11:30 Session 4**
 - Refinement (Less Pain and Distress) of Animal Use for Botulinum Toxin Potency Testing
- **11:30-12:30 Lunch**
- **12:30-2:20 Session 5**
 - Reduction of Animal Use for *In Vivo* Botulinum Testing
- **2:35-3:35 Session 6**
 - Wrap-up of Discussions
- **3:35-4:00 Closing Comments**

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ICCVAM Biologics Working Group

CDC	Joanne Andreadis, Ph.D. Susan Maslanka, Ph.D.	FDA	Suzanne Fitzpatrick, Ph.D. Dave Hattan, Ph.D. Abby Jacobs, Ph.D.* James Keller, Ph.D. Richard McFarland, M.D., Ph.D. Amy Rosenberg, M.D. Leonard Schechtman, Ph.D. Shashi Sharma, Ph.D. Elizabeth Shores, Ph.D. Richard Whiting, Ph.D.
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DOD	Leonard Smith, Ph.D.		
DOI	Tonie Rocke, Ph.D.		
EPA	Karen Hamernik, Ph.D. Chandrika Moudgal, M.S. Ram Ramabhadran, Ph.D. Amy Rispin, Ph.D.	NIEHS	William Stokes, D.V.M. Raymond Tice, Ph.D.
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NICEATM Staff

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Debbie McCarley	Special Assistant; Asst. Project Officer

Center Support Contract (ILS, Inc.)

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